# Editorial The Right Ventricle is No Longer the Forgotten Ventricle: Protecting & Managing It

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#### Introduction

When I was in my training years ago, not much attention was paid to protecting the right ventricle (RV) nor to enhancing its function. I can recall my mentors describing the RV as "just a giant vein". Over the years it became apparent that the right ventricle deserved more respect and attention than many had paid to both its protection and its function. One example of this change in focus was related to Dr. William Norwood's developing his strategy, the eponymous 'Norwood Procedure', for dealing with babies born with the Hypoplastic Left Heart Syndrome, in which the right heart becomes the single ventricle supporting both the pulmonary and the systemic circulations. Another evolution in thinking about the right ventricle occurred along with the development and use of left ventricular assist devices (LVADs), in which the right ventricle must maintain the pulmonary circulation, while an LVAD maintains the systemic circulation. And, in the realm of heart transplantation, it also became apparent that the right ventricle, not infrequently, struggled to function optimally when a donor heart was transplanted into a patient who often had a higher than normal pulmonary arterial resistance. Therefore, in more recent times, we have had to learn more about protecting the right ventricle and assisting its function in a variety of situations. There are quite a few issues to consider in this realm, and we will address the most important of those issues here. Let's get started.....

# Protecting the Right Ventricle during & after Cardiac Surgery

#### Preparing to Protect the RV Prior to a Planned Cardiac Operation

I have long believed in the value of sending out an email the afternoon or evening prior to a cardiac surgical operation. In such an email, I want to alert all on the cardiac surgery team of the plans for the anticipated operation and of supplies, medications, or devices that might be needed. Notifications of this sort are enhanced by the use of standardized checklists and protocols. I like to describe these

preparations as having "a talismanic" and positive effect on improving the outcomes of anticipated procedures.

#### Protecting the RV during Cardiac Surgery

While strategies for protecting the left ventricle are well known, there has been relatively less attention paid specifically to protecting the right ventricle during cardiac surgery. The primary issues in protecting the RV during cardiac surgery are physical factors and ischemia. The physical factors that may compromise RV function include stretch injury and external pressure, both of which can be avoided, at least to some degree. Ischemic injury can be ameliorated in a variety of ways, as well. We will discuss each of these types of injuries in turn.

Stretch injury can be avoided by managing the filling of the RV, during operations as well as during the postoperative period. During cardiac surgical operations, both bi-caval cannulation and venting of the pulmonary artery can help prevent over-filling of the RV. Obviously, bi-caval cannulation, especially with the taping of the venous cannulas, will control RV filling. This control of RV filling can be enhanced by venting the pulmonary artery (PA) in some manner. Another consideration, when completing a cardiac surgical operation is to simply wean slowly off of cardiopulmonary bypass while carefully watching and regulating the filling of the RV.

Physical injury (other than stretch injury) to the RV can occur intraoperatively when positioning the heart for bypass grafting of lateral or inferior wall coronary arteries. Having an assistant hold the heart when exposing those target vessels can be made safer and more effective if a dry gauze or lap pad is used to maintain optimal traction on the heart. Some surgeons even have their assistants wear sterile cloth outer gloves for this purpose. Creating friction on the surface of the heart will allow it to be positioned with less pressure on the myocardium than would otherwise be possible.

Physical injury to the RV can also occur during open cardiac massage, of course. I first witnessed this type of injury when working as a resident in the burn unit in my hospital and a patient's chest had been opened to perform open cardiac massage. Suddenly, blood shot out of the chest striking the nearby wall. The surgeon performing the open

massage said "well, we're done here" as he walked away from the bedside. I did not know then what I do know now: he was correct. That injury was not salvageable under those conditions. I did learn later that, when performing open cardiac massage, you should use two hands to avoid the "thumb injury" to the distended RV that seemed to have occurred in that patient.

Ischemic injury to the RV during cardiac surgical operations, while receiving considerably less attention than ischemic injury to the left ventricle (LV), remains an important issue. First of all, consideration may occasionally need to be given to grafting a sizable coronary artery that supplies the right ventricle, if significant atherosclerotic disease is present. The protection of the RV myocardium from ischemic injury can, of course, also be enhanced by the optimal delivery of cardioplegia. This delivery is best accomplished with the use of a DLP cardioplegia cannula inserted into the intact aortic root during aortic cross-clamping, as long as the root is not opened for a portion of the planned operation, such as for an aortic valve replacement, and assuming that the aortic valve (native or prosthetic) is competent. If this route of delivery of cardioplegia is not feasible, the aortic root can be partially opened to provide access to the individual coronary ostia, for the infusion of cardioplegia into those coronary ostia. If the right coronary artery is non-dominant, a pediatric coronary cannula can often be used to infuse cardioplegia into that generally smaller coronary ostium.

If a retrograde coronary sinus catheter will be used for the delivery of cardioplegia, a snare can be placed around the proximal end of the coronary sinus externally, close to its site of entry into the right atrium, which will enhance delivery of cardioplegia to the veins that ordinarily drain the right ventricle [1]. Placing such a suture around the coronary sinus is safe and easily done after the coronary sinus catheter has been placed. While some surgeons will pull the coronary sinus catheter back from its usual position deeper in that sinus after placing a suture around the proximal portion of the sinus, this maneuver is not necessary, as can be discerned by observing the filling of the veins that ordinarily drain the myocardium of the right ventricle during cardioplegia infusion, regardless of whether that coronary sinus catheter is pulled back or not. If the right coronary artery is diseased, and a bypass to it is planned, constructing this graft before other grafts should be considered, as that graft can then be connected to a multi-head cardioplegia setup to deliver cardioplegia to the myocardium served by that coronary artery. If the right atrium will be opened during the case, a pursestring stitch can be placed, temporarily, around the coronary sinus ostium inside the atrium, to enhance the delivery of cardioplegia to the RV, though the external snare placed around the proximal coronary sinus works just as well.

The right ventricular myocardium can also be protected from ischemia that can be exacerbated by rewarming during an operation by the use of bi-caval cannulation, which will lessen the rewarming caused by the venous return of systemic blood to the heart. The effectiveness of this bi-caval cannulation can be enhanced, of course, by the use of caval tapes which will prevent the warm systemic blood from having direct contact with the right ventricular muscle. These tapes can be easily placed by pulling up on the venous cannulae after insertion and using the cautery in a pin point fashion to create a tiny hole in the pericardial reflections that surround the cavae, taking care not to injure the posterior aspect of the cavae.

#### Protecting the RV after Cardiac Surgery

The physical protection of the RV after cardiac surgery should actually start early in most cardiac operations, when opening the pericardium. A technique for opening the pericardium, that was described by Dr. John Flege to optimize coverage of an internal mammary artery graft, can also be used to protect the anterior surface of the right ventricle, especially when the chest may need to be left open after a cardiac operation [2]. In fact, once I learned about this method of opening the pericardium, I used it for every cardiac surgical operation that I performed for decades.

One way that the external pressure on the RV after a cardiac surgical operation can be managed is by paying attention to how the pericardium is closed or reapproximated, as its closure, by definition, may create at least a bit of compression of the RV. If one opens the anterior pericardium more towards the left side rather than in the midline, as mentioned above, the resulting pericardial flap can be loosely stitched to the pericardial fat on the left side of the mediastinum or that pericardial flap can be extended by utilizing a prosthetic pericardial substitute, such as polytetrafluoroethylene (PTFE) or bovine pericardium.

Pressure on the RV that can result from the accumulation of blood or fluid in the pericardial space may also be alleviated or prevented by optimizing the drainage of blood and fluid from the pericardial space. One way to enhance pericardial drainage is to cut a hole in the posterior pericardium so that the pericardial fluid or blood can drain into the left pleural space. You must be aware of the location of the phrenic nerve at all times when incising the posterior pericardium, of course, to avoid injuring that nerve. Placing a Blake drain behind the heart, through such a pericardiotomy, and into the left pleural space will help accomplish this type of drainage quite effectively. Finally, I have always been guided by the old quip that "everyone is a potential reop, sooner or later". I have added a corollary to that saying by regularly asserting my strong belief that "the anterior surface of the heart and the sternum should never, ever, be in contact with each other".

In protecting the RV from ischemic injury, consideration should always be given to managing oxygen delivery to the myocardium of both ventricles, with attention to the hemoglobin level or the hematocrit, both during the operation and postoperatively as well, since ischemia of the myocardium interferes with optimal relaxation of the myocardium during diastole. While there are times when a restrictive transfusion strategy may be necessary, as with patients who will not accept blood transfusions (such as patients who are Jehovah's Witnesses), most cardiac surgery teams seek to maintain what they consider to be a reasonable hematocrit or hemoglobin level. When I am asked about my preferred parameters for these levels, I like to use the quip that "I go with God and Darwin" to convey my instinct that more oxygen carrying capacity is generally optimal for cardiac protection and performance.

One type of "oxygen delivery" that should be avoided is, of course, air embolism! The operative field can be flooded with  $CO_2$ , as it is much more soluble in blood than is air, which is, of course ~80% nitrogen, which is very poorly soluble compared to CO<sub>2</sub> or oxygen. Furthermore,  $CO_2$  is heavier than air (as we know from the use of fire extinguishers), so it will tend to 'sink into' the open chest. For this reason, I have frequently used CO2 insufflation into the chest cavity in cardiac surgical cases, especially those in which the heart itself is open (in contrast to cases like coronary artery bypass grafting, where the heart itself is rarely open). It is also important to 'deair' the heart in cases in which the chambers of the heart have been opened. Venting the aorta is a crucial part of 'scavenging' air that has entered the left side of the heart, of course. Air in the apex of the LV can be vented by simply passing a large bore needle into the apex of the LV, usually at the end of the procedure being done, a process we like to call "burping the heart". Furthermore, the adequacy of the deairing can be monitored with echocardiography.

#### Protecting the RV during Reoperations

We have addressed the issues of protecting the heart during reoperations in a prior two-part treatise on that subject, so we will refer the reader to those articles [3,4].

### **Managing Right Ventricular Function**

#### Preoperative Strategies to Enhance RV Function

There are several strategies that can be employed preoperatively to enhance the function of the right ventricle following cardiac surgical operations. These strategies include the use of diuretics to achieve an optimal volume status, sildenafil to lower pulmonary resistance, the use of a spirometer to optimally expand the lungs and to teach the patient how to use this device, and the optimization of a patient's nutritional status, when time permits.

# The Five Issues that Determine RV Function during and after Cardiac Surgery

A useful approach to optimizing the output of both the right and left ventricles is to consider how well the heart fills, how well it empties, and the electrical state of the heart [5]. The factors that determine how well the heart fills include both preload and the compliance of the ventricles. The factors that determine how well the heart empties include the inotropic state of the ventricular muscle and the afterload the heart is pumping against. And, the heart rate and rhythm will influence both the filling and the emptying of the ventricles. In addition to these general principles, the delivery of oxygenated blood to the ventricular muscle and the status of the valves of the heart are important factors in how the ventricles perform. We will address how each of these issues affects the performance of the right ventricle (as well as that of the left ventricle), while recognizing that some of these factors are important in more than one aspect of right ventricular function.

#### Managing the Preload of the RV

While the primary focus in managing the preload of the right ventricle will be based on the central venous pressure, echo guidance can also be useful to determine optimal filling and function of the RV (as well as of the LV, of course). These methods of monitoring can be supplemented by measuring cardiac output with a Swan Ganz catheter. The optimal technique of monitoring with a Swan Ganz catheter is with continuous monitoring of cardiac output using oximetry, which has become widely available in recent years. This type of monitoring is more useful in the postoperative period, especially when guidance from echocardiography may no longer be available. Obviously, tricuspid valve insufficiency will compromise the preload available to the RV, and consideration must be given to repairing that valve if regurgitation through it is significant. And, finally, in the setting of the implantation of a left ventricular assist device (LVAD), managing the output of that LVAD can play a role in the preload of the RV. That is, if an LVAD is pumping too much blood, the venous return can overwhelm a struggling RV.

#### Managing the Compliance of the RV

There are two primary issues to focus on when considering the compliance of the right ventricle, or how well the right ventricle fills during diastole, which are external pressure on the ventricle and the intrinsic compliance of the ventricle itself.

Optimal management of the pericardial space is crucial to avoiding tamponade physiology that can impair the filling of the RV. I have already mentioned the role of The Flege Flap in protecting the RV from physical injury, while avoiding compression from the pericardial reconstruction. The pericardial space must also be drained optimally. Many surgeons believe that Blake drains are the best type of drains to use for drainage of the pericardium, as it is rare for those drains to be completely obstructed by clotted blood. Some surgeons will use as many as four or five of these drains to ensue optimal drainage not only of the pericardium but also of the pleural spaces. At least one of these drains should be positioned in the posterior pericardial space. I adopted the practice of making small openings in the pericardial reflections beneath both cavae, so that I could have one of these drains positioned so that it "circled" around in the pericardial space behind the heart. I also adopted the practice of creating a posterior pericardiotomy and directing a Blake drain through it and into the left pleural space, as mentioned earlier. To reiterate, it is imperative to minimize the accumulation of blood or fluid around the heart to preserve optimal filling of the right ventricle.

While the most obvious source of external pressure on the RV is tamponade caused by the accumulation of blood or fluid around the heart, there are other factors that can impair the filling of the RV, including pressure from the closure of the pericardium or of the chest (which may be worsened by edema) and high pressure from ventilation, especially when the lungs themselves are edematous or stiff. These issues have well known solutions, such as leaving the chest open temporarily, if closing the chest causes compression when attempted, or the temporary use of extracorporeal membrane oxygenation (ECMO) to supplement or replace standard ventilation strategies.

Pressure on the RV resulting from the closure of the sternotomy can be avoided, in the early postoperative period, by leaving the sternotomy open temporarily. Keeping the sternum open and at last slightly distanced from the RV can be accomplished with the use of struts (usually made from syringe barrels tailored to fit and stay in place with the use of an eye cautery). This approach can be supplemented, or possibly replaced, by the use of a VAC Sponge positioned between the sternal edges, in some situations [6].

Planned reexploration to 'wash out' the chest and to close the sternotomy can be done safely in the intensive care when the patient's condition has stabilized postoperatively [7]. As mentioned earlier, there are strategies that are worth considering in the management of the pericardium that can be helpful in covering the anterior surface of the RV, not only to minimize pressure on the heart but also to protect it, either during a time when the chest may need to be left open or at the time of a subsequent operation.

An issue related to ventricular compliance that is less commonly considered is ischemia of the myocardium, as adequate oxygen delivery is crucial to maintaining optimal relaxation (i.e., the compliance) of the right ventricular myocardium, as well as to optimizing its systolic function. While there are many factors that may be considered when attempting to enhance the delivery of oxygen to the RV myocardium, one that should be emphasized is the possibility of revascularizing its coronary branches, if one or more of them is compromised and large enough to bypass with an appropriate conduit, as noted above. Obviously, there are other, well known, factors to consider in optimizing oxygen delivery to all organs in the body, such as maintaining proper oxygen carrying capacity of the blood by, for example, transfusing the patient when indicated.

Another issue that needs to be considered in optimizing oxygen delivery to the myocardium (of both ventricles) is the diastolic pressure of the systemic circulation, as it is during diastole that the myocardium is perfused. Obviously, if significant regurgitation of the aortic valve is present, diastolic pressure will be lower and, if that pressure seems to be inadequate for optimal coronary perfusion, consideration can be given to repairing or replacing the aortic valve. Similarly, there may be occasions when an intraaortic balloon pump can be used to support the diastolic pressure to enhance perfusion of the RV myocardium. On a related note, it is not uncommon in sick patients for there to be an element of peripheral vasodilation that may compromise coronary perfusion. This vasodilatation can often be managed by the use of vasopressin.

# Managing How Well the RV Empties: The Inotropic State of the RV

Managing the inotropic state of the right ventricle is, of course, inextricably linked to managing the inotropic state of the left ventricle, unless, of course, the challenge in the moment is optimizing right ventricular performance after the implantation of a left ventricular assist device (LVAD). In the setting of LVAD implantation, virtually all of your attention will be focused on optimizing the performance of the right ventricle, obviously. While there are advantages and disadvantages of various inotropes, and combinations of these agents, my favorite inotropes became, over many decades of practice, a combination of milrinone and norepinephrine. These inotropes not only work synergistically, they are also fairly easy to titrate to the desired effect. And, while milrinone can cause some vasodilatation, the use of norepinephrine will allow you to maintain the systemic blood pressure at an optimal level. Of note, neither of these inotropes have much, if any, propensity to raise the pulmonary vascular resistance. Furthermore, neither of these medications are chronotropes, which will minimize the likelihood of arrhythmias while allowing you to maintain control of the heart rate with pacing wires and an external pacemaker, which we will address below.

Another consideration in optimizing the inotropic state of the heart is to manage the utilization of glucose, which is, of course, the primary fuel of the heart. Hyperglycemia is common in many sick cardiac surgical patients and some inotropes, such as epinephrine, may exacerbate this condition. For this reason, one can consider using an insulin drip which will enhance glucose utilization, even in the myocardium (which is traditionally thought not to require insulin for glucose utilization). In fact, I eventually came to the conclusion that an insulin drip should be used routinely for patients in whom I was implanting an LVAD. While some have advocated using a glucose, insulin, and potassium drip in heart failure patients, I have found that using an insulin drip alone is a simpler, and usually sufficient, approach, being easier to set up and to titrate precisely, based on the measured glucose levels.

# The Valves of the RV are also Important in Managing its Function

As noted earlier, significant insufficiency of the tricuspid valve should be addressed with some form of valvuloplasty in most patients, with my own preference being the implantation of a prosthetic annuloplasty ring, though some prefer other annuloplasty techniques. And, though rarely present in adults without congenital cardiac malformations, you must also ensure that the pulmonary valve is functioning reasonably well, which might require a patch to enlarge its orifice, while the need to replace that valve is rare in this setting [8].

### Managing the Electrical State of the RV

It is apparent that having, or creating, normal sinus rhythm, with an optimal heart rate, is one the goals of optimally managing the function of the right ventricle. The optimal heart rate may differ from patient to patient for various reasons, but generally that rate will be between 70 and 90 beats per minute. Furthermore, establishing and maintaining a regular rhythm, with atrioventricular synchronization, is also a priority in maintaining optimal function of both ventricles. If atrial or ventricular arrhythmias are present, a regular rhythm can be restored with the use of defibrillation, which is, of course, generally straightforward when the patient is still in the operating room with the chest open. The placement of temporary pacing cardiac wires will allow optimal control of the heart rate and, possibly, suppress arrhythmias. It is worth noting that, if atrial pacing alone is sufficient, that pacing strategy can improve ventricular function, as electrical impulses that 'flow' through the intrinsic conduction system will enhance ventricular function. Finally, the pacing rate, and sometimes the location of the wires, can be optimized with the use of echocardiography [9].

#### Managing the Afterload of the RV

The afterload 'faced' by the right ventricle is an important factor affecting its performance. Obviously, in the setting of some degree of stenosis of the pulmonary valve, consideration can be given to dealing with that condition, which could include repairing or replacing that valve, as noted earlier. This condition is unusual, at least in most adult patients.

However, there are other strategies that can be employed prior to, during, or after a cardiac surgical operation to reduce afterload experienced by the RV. Preoperative interventions to reduce pulmonary vascular resistance (PVR) can include adequate diuresis and the preoperative administration of sildenafil, which is a fairly selective pulmonary arterial vasodilator (though it can have some mild systemic effect, as well). During the operation, and afterwards as well, keeping the PCO<sub>2</sub> low and the PO<sub>2</sub> high will help keep the PVR low. Intraoperative administration of nitroglycerine has also been used for this purpose, and, if it is used, it should be started prior to beginning to wean from CPB. However, this medication does cause inhibition of platelet function and, while it affects the pulmonary arterial resistance, it also lowers peripheral arterial resistance, at least to some degree [10]. For these reasons, inhaled pulmonary vasodilators are generally preferred, at least while the patient is being ventilated. One of the first medications used for this purpose was inhaled nitric oxide [11]. However, after the introduction of this therapy, some 'enterprising individuals' found a way to patent the use of this common gas, which, nearly overnight, made its use prohibitively expensive. Therefore, alternative, less expensive, inhaled vasodilators were found and employed widely. These medications are mostly congeners of prostacyclin, such as epoprostenol [12].

It is recognized that "transfusion related acute lung injury" (TRALI) can contribute to increased pulmonary vascular resistance. However, while you may be able to use a restrictive transfusion strategy in some patients, there will be many patients in which the transfusion of blood products will be necessary. Some clinicians believe that the use of blood filters may lessen the effects on the pulmonary circulation of transfusions, but this strategy is somewhat controversial and is also sometimes impractical.

It is also worth noting that high airway pressures can add resistance to the RV output, so working to lower these pressures can also help optimize the RV output. One approach to manage excessive airway pressures is to include an oxygenator in any mechanical circulatory support system that might be utilized, as this technique will ensure adequate oxygenation and promote lowering of the pulmonary arterial resistance, while possibly also reducing the airway pressure that might have seemed necessary to optimize oxygenation.

#### Supplementing RV Output, When Necessary

Obviously, if or when all these interventions are inadequate, temporary mechanical assistance of right ventricular output will need to be implemented with the use of a right ventricular assist device (RVAD). We developed a fairly simple strategy for instituting this kind of RVAD support, which entails the use of a percutaneously placed right femoral venous cannula and a graft sewn to the pulmonary artery, which can be led out of the chest through the left second intercostal space, and attached to the arterial cannula of a right ventricular assist device (RVAD). This strategy allows the chest to be closed as the operation concludes. When the right ventricular function has recovered adequately, as demonstrated by echocardiography and hemodynamic measurements, these cannulas can be easily removed at the bedside in the intensive care unit. We have described this technique in detail in prior publications [13,14].

It is worth noting that, if a temporary RVAD is needed, you should consider using it for several days after the operation to allow adequate time for RV recovery, diuresis, and the fine tuning of various medications. Finally, it is worth noting that utilizing an RVAD may shorten the time spent in the operating room after an LVAD implant, and it may also decrease persistent venous oozing by reducing the central venous pressure.

# Management of the RV after LVAD Implantation

One must pay careful attention to the LVAD flows after implantation, because keeping the LVAD flows down as much as possible may help avoid the overfilling of the RV. Attention must also be given to minimizing RV ischemia, especially by avoiding air emboli to the coronaries supplying the RV, as much as feasible, and by maintaining adequate systemic diastolic pressure, as the coronaries supplying the RV myocardium are perfused primarily during diastole, as noted earlier.

#### Why do the Right Ventricles of Hearts Procured for Transplantation not Always Work Optimally?

It is quite common to see the right ventricles of hearts procured for transplantation struggle when implanted into the patient receiving that heart. I have long wondered about the source of this dysfunction, which is usually transient. While some will invoke the generally high pulmonary vascular resistance in the recipients who have, of course, been in a state of congestive heart failure, this RV dysfunction is common even in recipients who have been supported with an LVAD and who, theoretically, are not in heart failure at the time of their transplant procedure. While I do not have an evidence-based explanation for this common condition, I do wonder if the explanation might be that, during procurement, the coronary arteries of the donor heart often end up filled with air. When a donor heart is removed from the chest of the donor, the blood or preservation solution that filled the coronary arteries and veins is often allowed to drain out, which may allow air to be drawn into the proximal coronary arteries, perhaps filling them with that air. It is well known that air that has made its way into arteries may remain in those vessels for quite some time. Some strategies that might ameliorate, or at least lessen, this entrainment of air in the coronary arteries of a donor heart include:

- Not removing the aortic cross clamp placed during the procurement.

- Stapling the ascending aorta rather than using a typical aortic clamp (so that the aorta remains full of the cardioplegia solution).

- Keeping the heart submerged in saline as much as possible during procurement, transport, and subsequent implantation.

- Keeping the heart in an 'apex up' position as much as might be feasible during both procurement and implantation, which might lessen the drainage of the cardioplegia solution from the aortic root and the subsequent entrainment of air bubbles in the coronary arteries.

- Adequate venting of the LV at the time of implantation of the transplanted heart.

#### Care of Patients Postoperatively

While there are a great many issues related to postoperative care of sick patients that could be discussed, there are several strategies that are worth mentioning, such as asking that the ICU room to which the patient will be transferred be warmed optimally prior to the patient's arrival and arranging for an air bed to be available for patients likely to be relatively immobile for a time. I have also liked to consider the use of 'trophic tube feedings' of the patient to ensure optimal nutrition and to 'manage the gut' postoperatively. Finally, I like to ask the team caring for the patients to 'be in no hurry' to wean to extubate these patients who may well 'need some time' to stabilize. The pertinent admonition is 'never move electively from a position of clinical stability to a position of instability.

#### Summary

In the current era of cardiac surgery, there are many useful strategies to protect, enhance, or supplement the function of the right ventricle, which we have summarized in this treatise. If the right ventricle was once "the forgotten ventricle", it no longer suffers from this ignominy.

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This manuscript was completed by CT, alone.

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# **Conflict of Interest**

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